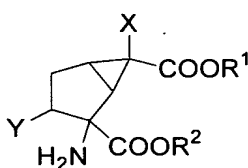


CLAIM

We claim:

1. A 2-amino-bicyclo [3.1.0] hexane-2,6-dicarboxylic acid derivative, a pharmaceutically acceptable salt thereof or a hydrate thereof, represented by formula [I]

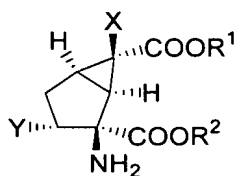


[I]

- [wherein R^1 and R^2 are the same or different, and each represents a hydrogen atom, a C_{1-10} alkyl group, a phenyl group, a naphthyl group, a C_{1-10} alkyl group substituted by one or two phenyl groups, a C_{2-10} alkenyl group, a C_{2-10} alkynyl group, a hydroxyl C_{2-10} alkyl group, a C_{1-10} alkoxycarbonyl C_{1-10} alkyl group, an amino C_{2-10} alkyl group or a C_{1-10} alkoxy C_{1-10} alkyl group;
- X represents a hydrogen atom or a fluorine atom;
- Y represents an amino group, $-SR^3$, $-S(O)_nR^7$, $-SCHR^3R^4$, $-S(O)_nCHR^3R^4$, $-NHCHR^3R^4$, $-N(CHR^3R^4)(CHR^5R^6)$, $-NHCOR^3$ or $-OCOR^7$ (wherein R^3 , R^4 , R^5 and R^6 are the same or different, and each represents a hydrogen atom, a C_{1-10} alkyl group, a phenyl group, a naphthyl group, a naphthyl group substituted by one to seven halogen atoms or a hetroaromatic group, or represents “a phenyl group substituted by one to five substituents selected from a group consisting of a halogen atom, a phenyl group, a C_{1-10} alkyl group, a C_{1-10} alkoxy group and a trifluoromethyl group”;
- R^7 represents a C_{1-10} alkyl group, a phenyl group, a naphthyl group, a naphthyl group substituted by one to seven halogen atoms or a hetroaromatic group, or represents “a phenyl group substituted by one to five substituents selected from a group consisting of a

halogen atom, a phenyl group, a C₁₋₁₀alkyl group, a C₁₋₁₀alkoxy group and a trifluoromethyl group”; and n represents integer 1 or 2)].

2. A 2-amino-bicyclo [3.1.0] hexane-2,6-dicarboxylic acid derivative, a pharmaceutically acceptable salt thereof or a hydrate thereof, represented by formula [II]



[II]

- [Wherein R¹ and R² are the same or different, and each represents a hydrogen atom, a C₁₋₁₀alkyl group, a phenyl group, a naphthyl group, a C₁₋₁₀alkyl group substituted by one or two phenyl groups, a C₂₋₁₀alkenyl group, a C₂₋₁₀alkynyl group, a hydroxylC₂₋₁₀alkyl group, a C₁₋₁₀alkoxycarbonylC₁₋₁₀alkyl group, an aminoC₂₋₁₀alkyl group or a C₁₋₁₀alkoxyC₁₋₁₀alkyl group;

X represents a hydrogen atom or a fluorine atom;

- Y represents an amino group, -SR³, -S(O)_nR⁷, -SCHR³R⁴, -S(O)_nCHR³R⁴, -NHCHR³R⁴, -N(CHR³R⁴)(CHR⁵R⁶), -NHCOR³ or -OCOR⁷ (wherein R³, R⁴, R⁵ and R⁶ are the same or different, and each represents a hydrogen atom, a C₁₋₁₀alkyl group, a phenyl group, a naphthyl group, a naphthyl group substituted by one to seven halogen atoms or a hetroaromatic group, or represents “a phenyl group substituted by one to five substituents selected from a group consisting of a halogen atom, a phenyl group, a C₁₋₁₀alkyl group, a C₁₋₁₀alkoxy group and a trifluoromethyl group”;

- R⁷ represents a C₁₋₁₀alkyl group, a phenyl group, a naphthyl group, a naphthyl group substituted by one to seven halogen atoms or a hetroaromatic group or represents “a phenyl group substituted by one to five substituents selected from a group consisting of a halogen atom, a phenyl group, a C₁₋₁₀alkyl group, a C₁₋₁₀alkoxy group and a trifluoromethyl group”; and n represents integer 1 or 2)].

3. A 2-amino-bicyclo [3.1.0] hexane-2,6-dicarboxylic acid derivative according to claim 2, a pharmaceutically acceptable salt thereof or a hydrate thereof, represented by formula [II], wherein R^2 represents a hydrogen atom.

5

4. A 2-amino-bicyclo [3.1.0] hexane-2,6-dicarboxylic acid derivative according to claim 2, a pharmaceutically acceptable salt thereof or a hydrate thereof, represented by formula [II], wherein R^1 and R^2 each represents a hydrogen atom.

10

5. A 2-amino-bicyclo [3.1.0] hexane-2,6-dicarboxylic acid derivative according to claim 2, a pharmaceutically acceptable salt thereof or a hydrate thereof, represented by formula [II], wherein R^1 and R^2 each represents a hydrogen atom; and
X represents a fluorine atom.

15

6. A 2-amino-bicyclo [3.1.0] hexane-2,6-dicarboxylic acid derivative according to claim 2, a pharmaceutically acceptable salt thereof or a hydrate thereof, represented by formula [II], wherein R^1 and R^2 each represents a hydrogen atom; and
X represents a hydrogen atom.

20

7. A 2-amino-bicyclo [3.1.0] hexane-2,6-dicarboxylic acid derivative according to claim 2, a pharmaceutically acceptable salt thereof or a hydrate thereof, represented by formula [II], wherein R^1 and R^2 each represents a hydrogen atom;
X represents a fluorine atom; and
Y represents $-SR^3$ ($-SR^3$ is the same as mentioned above).

25

8. A 2-amino-bicyclo [3.1.0] hexane-2,6-dicarboxylic acid derivative according to claim 2, a pharmaceutically acceptable salt thereof or a hydrate thereof, represented by formula [II], wherein R^1 and R^2 each represents a hydrogen atom;
X represents a fluorine atom; and

Y represents $-S(O)_nR^7$ ($-S(O)_nR^7$ is the same as mentioned above).

9. A 2-amino-bicyclo [3.1.0] hexane-2,6-dicarboxylic acid derivative according to claim 2, a pharmaceutically acceptable salt thereof or a hydrate thereof, represented by formula [II], wherein R^1 and R^2 each represents a hydrogen atom;

X represents a fluorine atom; and

Y represents $-SCHR^3R^4$ ($-SCHR^3R^4$ is the same as mentioned above).

10. A 2-amino-bicyclo [3.1.0] hexane-2,6-dicarboxylic acid derivative according to claim 2, a pharmaceutically acceptable salt thereof or a hydrate thereof, represented by formula [II], wherein R^1 and R^2 each represents a hydrogen atom;

X represents a fluorine atom; and

Y represents $-S(O)_nCHR^3R^4$ ($-S(O)_nCHR^3R^4$ is the same as described above).

11. A 2-amino-bicyclo [3.1.0] hexane-2,6-dicarboxylic acid derivative according to claim 2, a pharmaceutically acceptable salt thereof or a hydrate thereof, represented by formula [II], wherein R^1 and R^2 each represents a hydrogen atom;

X represents a fluorine atom; and

Y represents $-NHCHR^3R^4$ ($-NHCHR^3R^4$ is the same as mentioned above).

20

12. A 2-amino-bicyclo [3.1.0] hexane-2,6-dicarboxylic acid derivative according to claim 2, a pharmaceutically acceptable salt thereof or a hydrate thereof, represented by formula [II], wherein R^1 and R^2 each represents a hydrogen atom;

X represents a fluorine atom; and

- 25 Y represents $-N(CHR^3R^4)(CHR^5R^6)$ ($-N(CHR^3R^4)(CHR^5R^6)$ is the same as mentioned above).

13. A 2-amino-bicyclo [3.1.0] hexane-2,6-dicarboxylic acid derivative according to claim 2, a pharmaceutically acceptable salt thereof or a hydrate thereof, represented by formula

[II], wherein R^1 and R^2 each represents a hydrogen atom;

X represents a fluorine atom; and

Y represents $-NHCOR^3$ ($-NHCOR^3$ is the same as mentioned above).

- 5 14. A 2-amino-bicyclo [3.1.0] hexane-2,6-dicarboxylic acid derivative according to claim 2, a pharmaceutically acceptable salt thereof or a hydrate thereof, represented by formula [II], wherein R^1 and R^2 each represents a hydrogen atom;
- X represents a fluorine atom; and
- Y represents $-OCOR^7$ ($-OCOR^7$ is the same as mentioned above).

10

15. A 2-amino-bicyclo [3.1.0] hexane-2,6-dicarboxylic acid derivative according to claim 2, a pharmaceutically acceptable salt thereof or a hydrate thereof, represented by formula [II], wherein R^1 and R^2 each represents a hydrogen atom;
- X represents a hydrogen atom; and

- 15 Y represents $-SR^3$ ($-SR^3$ is the same as mentioned above).

16. A 2-amino-bicyclo [3.1.0] hexane-2,6-dicarboxylic acid derivative according to claim 2, a pharmaceutically acceptable salt thereof or a hydrate thereof, represented by formula [II], wherein R^1 and R^2 each represents a hydrogen atom;

- 20 X represents a hydrogen atom; and

Y represents $-S(O)_nR^7$ ($-S(O)_nR^7$ is the same as mentioned above).

17. A 2-amino-bicyclo [3.1.0] hexane-2,6-dicarboxylic acid derivative according to claim 2, a pharmaceutically acceptable salt thereof or a hydrate thereof, represented by formula

- 25 [II], wherein R^1 and R^2 each represents a hydrogen atom;

X represents a hydrogen atom; and

Y represents $-SCHR^3R^4$ ($-SCHR^3R^4$ is the same as mentioned above).

18. A 2-amino-bicyclo [3.1.0] hexane-2,6-dicarboxylic acid derivative according to claim

2, a pharmaceutically acceptable salt thereof or a hydrate thereof, represented by formula [II], wherein R^1 and R^2 each represents a hydrogen atom;

X represents a hydrogen atom; and

Y represents $-S(O)_nCHR^3R^4$ ($-S(O)_nCHR^3R^4$ is the same as mentioned above).

5

19. A 2-amino-bicyclo [3.1.0] hexane-2,6-dicarboxylic acid derivative according to claim 2, a pharmaceutically acceptable salt thereof or a hydrate thereof, represented by formula [II], wherein R^1 and R^2 each represents a hydrogen atom;

X represents a hydrogen atom; and

10 Y represents $-NHCHR^3R^4$ ($-NHCHR^3R^4$ is the same as mentioned above).

20. A 2-amino-bicyclo [3.1.0] hexane-2,6-dicarboxylic acid derivative according to claim 2, a pharmaceutically acceptable salt thereof or a hydrate thereof, represented by formula [II], wherein R^1 and R^2 each represents a hydrogen atom;

15 X represents a hydrogen atom; and

Y represents $-N(CHR^3R^4)(CHR^5R^6)$ ($-N(CHR^3R^4)(CHR^5R^6)$ is the same as mentioned above).

21. A 2-amino-bicyclo [3.1.0] hexane-2,6-dicarboxylic acid derivative according to claim 2, a pharmaceutically acceptable salt thereof or a hydrate thereof, represented by formula [II], wherein R^1 and R^2 each represents a hydrogen atom;

20 X represents a hydrogen atom; and

Y represents $-NHCOR^3$ ($-NHCOR^3$ is the same as mentioned above).

25 22. A 2-amino-bicyclo [3.1.0] hexane-2,6-dicarboxylic acid derivative according to claim 2, a pharmaceutically acceptable salt thereof or a hydrate thereof, such a compound of formula [II] being:

(1R,2S,3R,5R,6R)-2-amino-3-(thiophene-2-ylmethylsulfanyl)-6-fluorobicyclo [3.1.0] hexane-2,6-dicarboxylic acid;

- (1R,2S,3R,5R,6R)-2-amino-3-(2-phenylbenzylsulfanyl)-6-fluorobicyclohexane-2,6-dicarboxylic acid; [3.1.0]
- (1R,2S,3R,5R,6R)-2-amino-3-(4-methoxybenzylsulfanyl)-6-fluorobicyclohexane-2,6-dicarboxylic acid; [3.1.0]
- 5 (1R,2S,3R,5R,6R)-2-amino-3-(4-fluorobenzylsulfanyl)-6-fluorobicyclohexane-2,6-dicarboxylic acid; [3.1.0]
- (1R,2S,3R,5R,6R)-2-amino-3-(4-*t*-butylbenzylsulfanyl)-6-fluorobicyclohexane-2,6-dicarboxylic acid; [3.1.0]
- (1R,2S,3R,5R,6R)-2-amino-3-(3-trifluoromethylbenzylsulfanyl)-6-fluorobicyclohexane-2,6-dicarboxylic acid; [3.1.0]
- 10 (1R,2S,3R,5R,6R)-2-amino-3-(1-bromo-naphthalene-2-ylmethylsulfanyl)-6-fluorobicyclohexane-2,6-dicarboxylic acid; [3.1.0]
- (1R,2S,3R,5R,6R)-2-amino-3-(3,4-dichlorobenzylsulfanyl)-bicyclohexane-2,6-dicarboxylic acid; [3.1.0]
- 15 (1R,2S,3R,5R,6R)-2-amino-3-(3,4-dichlorobenzylsulfanyl)-6-fluorobicyclohexane-2,6-dicarboxylic acid; [3.1.0]
- (1R,2S,3R,5R,6R)-2-amino-3-(3,4-dichlorobenzylsulfinyl)-6-fluorobicyclohexane-2,6-dicarboxylic acid; [3.1.0]
- (1R,2S,3R,5R,6R)-2-amino-3-(3,4-dichlorobenzylsulfonyl)-6-fluorobicyclohexane-2,6-dicarboxylic acid; [3.1.0]
- 20 (1R,2S,3R,5R,6R)-2-amino-3-(3,4-dichlorophenylsulfanyl)-6-fluorobicyclohexane-2,6-dicarboxylic acid; [3.1.0]
- (1R,2S,3R,5R,6R)-2-amino-3-(3-chloro-2,6-difluorobenzylsulfanyl)-6-fluorobicyclohexane-2,6-dicarboxylic acid; [3.1.0]
- 25 (1R,2S,3R,5R,6R)-2-amino-3-(propylsulfanyl)-6-fluorobicyclohexane-2,6-dicarboxylic acid; [3.1.0]
- (1R,2S,3R,5R,6R)-2-amino-3-(1-phenyl-ethylsulfanyl)-6-fluorobicyclohexane-2,6-dicarboxylic acid; [3.1.0]
- (1R,2S,3R,5R,6R)-2-amino-3-[bis-(4-fluorophenyl)methylsulfanyl]-6-fluorobicyclohexane-2,6-dicarboxylic acid; [3.1.0]

[3.1.0] hexane-2,6-dicarboxylic acid;

(1R,2R,3R,5R,6R)-2,3-diamino-6-fluorobicyclo [3.1.0] hexane-2,6-dicarboxylic acid;

(1R,2R,3R,5R,6R)-2-amino-3-(3,4-dichlorobenzylamino)-6-fluorobicyclo [3.1.0]
hexane-2,6-dicarboxylic acid;

5 (1R,2R,3R,5R,6R)-2-amino-3-[N,N-(3,4-dichlorobenzyl)methylamino]-6-fluorobicyclo
[3.1.0] hexane-2,6-dicarboxylic acid;

(1R,2R,3R,5R,6R)-2-amino-3-(3,4-dichlorobenzoylamino)-6-fluorobicyclo [3.1.0]
hexane-2,6-dicarboxylic acid; or

(1R,2R,3R,5R,6R)-2-amino-3-(3,4-dichlorobenzoyloxy)-6-fluorobicyclo [3.1.0]

10 hexane-2,6-dicarboxylic acid.

23. A 2-amino-bicyclo [3.1.0] hexane-2,6-dicarboxylic acid derivative according to claim 2, a pharmaceutically acceptable salt thereof or a hydrate thereof, such a compound of formula [II] being:

15 (1R,2R,3R,5R,6R)-2,3-diamino-6-fluorobicyclo [3.1.0] hexane-2,6-dicarboxylic acid
diethyl ester;

(1R,2S,3R,5R,6R)-2-amino-3-(thiophene-2-ylmethylsulfanyl)-6-fluorobicyclo [3.1.0]
hexane-2,6-dicarboxylic acid diethyl ester;

(1R,2S,3R,5R,6R)-2-amino-3-(2-phenylbenzylsulfanyl)-6-fluorobicyclo [3.1.0]

20 hexane-2,6-dicarboxylic acid diethyl ester;

(1R,2S,3R,5R,6R)-2-amino-3-(4-methoxybenzylsulfanyl)-6-fluorobicyclo [3.1.0]

hexane-2,6-dicarboxylic acid diethyl ester;

(1R,2S,3R,5R,6R)-2-amino-3-(4-fluorobenzylsulfanyl)-6-fluorobicyclo [3.1.0]

hexane-2,6-dicarboxylic acid diethyl ester;

25 (1R,2S,3R,5R,6R)-2-amino-3-(4-t-butylbenzylsulfanyl)-6-fluorobicyclo [3.1.0]

hexane-2,6-dicarboxylic acid diethyl ester;

(1R,2S,3R,5R,6R)-2-amino-3-(3-trifluoromethylbenzylsulfanyl)-6-fluorobicyclo [3.1.0]

hexane-2,6-dicarboxylic acid diethyl ester;

(1R,2S,3R,5R,6R)-2-amino-3-(1-bromo-naphthalene-2-ylmethylsulfanyl)-6-fluorobicycl

- o [3.1.0] hexane-2,6-dicarboxylic acid diethyl ester;
 (1R,2S,3R,5R,6R)-2-amino-3-(3,4-dichlorobenzylsulfanyl)-bicyclo [3.1.0]
 hexane-2,6-dicarboxylic acid 2-benzyl ester 6-ethyl ester;
 (1R,2S,3R,5R,6R)-2-amino-3-(3,4-dichlorobenzylsulfanyl)-6-fluorobicyclo [3.1.0]
- 5 hexane-2,6-dicarboxylic acid diethyl ester;
 (1R,2S,3R,5R,6R)-2-amino-3-(3,4-dichlorobenzylsulfinyl)-6-fluorobicyclo [3.1.0]
 hexane-2,6-dicarboxylic acid diethyl ester;
 (1R,2S,3R,5R,6R)-2-amino-3-(3,4-dichlorobenzylsulfonyl)-6-fluorobicyclo [3.1.0]
 hexane-2,6-dicarboxylic acid diethyl ester;
- 10 (1R,2S,3R,5R,6R)-2-amino-3-(3,4-dichlorophenylsulfanyl)-6-fluorobicyclo [3.1.0]
 hexane-2,6-dicarboxylic acid diethyl ester;
 (1R,2S,3R,5R,6R)-2-amino-3-(3-chloro-2,6-difluorobenzylsulfanyl)-6-fluorobicyclo
 [3.1.0] hexane-2,6-dicarboxylic acid diethyl ester;
 (1R,2S,3R,5R,6R)-2-amino-3-(propylsulfanyl)-6-fluorobicyclo [3.1.0]
- 15 hexane-2,6-dicarboxylic acid diethyl ester;
 (1R,2S,3R,5R,6R)-2-amino-3-(1-phenyl-ethylsulfanyl)-6-fluorobicyclo [3.1.0]
 hexane-2,6-dicarboxylic acid diethyl ester;
 (1R,2S,3R,5R,6R)-2-amino-3-[bis-(4-fluorophenyl)methylsulfanyl]-6-fluorobicyclo
 [3.1.0] hexane-2,6-dicarboxylic acid diethyl ester;
- 20 (1R,2R,3R,5R,6R)-2-amino-3-(3,4-dichlorobenzylamino)-6-fluorobicyclo [3.1.0]
 hexane-2,6-dicarboxylic acid diethyl ester;
 (1R,2R,3R,5R,6R)-2-amino-3-[N,N-(3,4-dichlorobenzyl)methylamino]-6-fluorobicyclo
 [3.1.0] hexane-2,6-dicarboxylic acid diethyl ester;
 (1R,2R,3R,5R,6R)-2-amino-3-(3,4-dichlorobenzoylamino)-6-fluorobicyclo [3.1.0]
- 25 hexane-2,6-dicarboxylic acid diethyl ester;
 (1R,2R,3R,5R,6R)-2-amino-3-(3,4-dichlorobenzoyloxy)-6-fluorobicyclo [3.1.0]
 hexane-2,6-dicarboxylic acid 2-benzyl ester 6-ethyl ester;
 (1R,2S,3R,5R,6R)-2-amino-3-(3,4-dichlorobenzylsulfanyl)-6-fluorobicyclo [3.1.0]
 hexane-2,6-dicarboxylic acid 2-ethyl ester;

(1R,2S,3R,5R,6R)-2-amino-3-(3,4-dichlorobenzylsulfanyl)-6-fluorobicyclo [3.1.0]
hexane-2,6-dicarboxylic acid 6-isobutyl ester; or

(1R,2S,3R,5R,6R)-2-amino-3-(3,4-dichlorobenzylsulfanyl)-6-fluorobicyclo [3.1.0]
hexane-2,6-dicarboxylic acid 6-benzyl ester.

5

24. A drug comprising the 2-amino-bicyclo [3.1.0] hexane-2,6-dicarboxylic acid derivative according to any one of claims 1 to 23, the pharmaceutically acceptable salt thereof or the hydrate thereof as an active ingredient.

10 25. The drug according to claim 24 wherein the drug is a Group II metabotropic glutamate receptor antagonist.